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**Stem cell maintenance by manipulating signaling pathways: past, current and future.**

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**Public Summary:**

Pluripotent stem cells only exist in a narrow window during early embryonic development, whereas multipotent stem cells are abundant throughout embryonic development and are retained in various adult tissues and organs. While pluripotent stem cell lines have been established from several species, including mouse, rat, and human, it is still challenging to establish stable multipotent stem cell lines from embryonic or adult tissues. Based on current knowledge, we anticipate that by manipulating different signaling pathways, most if not all types of stem cells can be maintained in a long-term culture. In this article, we summarize current culture conditions established for the long-term maintenance of pluripotent and multipotent stem cells and the signaling pathways involved. We also discuss the general principles of stem cell maintenance and propose several strategies on the establishment of novel stem cell lines through manipulation of signaling pathways.

**Scientific Abstract:**

Pluripotent stem cells only exist in a narrow window during early embryonic development, whereas multipotent stem cells are abundant throughout embryonic development and are retained in various adult tissues and organs. While pluripotent stem cell lines have been established from several species, including mouse, rat, and human, it is still challenging to establish stable multipotent stem cell lines from embryonic or adult tissues. Based on current knowledge, we anticipate that by manipulating extrinsic and intrinsic signaling pathways, most if not all types of stem cells can be maintained in a long-term culture. In this article, we summarize current culture conditions established for the long-term maintenance of authentic pluripotent and multipotent stem cells and the signaling pathways involved. We also discuss the general principles of stem cell maintenance and propose several strategies on the establishment of novel stem cell lines through manipulation of signaling pathways.

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